

**Definition**

We measure serum total CO<sub>2</sub> content in lieu of measuring serum bicarbonate. The total CO<sub>2</sub> content includes the serum bicarbonate as well as available forms of carbon dioxide (i.e., dissolved CO<sub>2</sub> and carbonic acid). Generally, the serum bicarbonate comprises about 95% of the total CO<sub>2</sub> content; thus we can use this measurement as an excellent estimator of serum bicarbonate. The total CO<sub>2</sub> content normally equals 23 to 30 mEq/L of serum.

**Technique**

Most laboratories use an autoanalyzer for measuring total CO<sub>2</sub> content. This method measures the amount of CO<sub>2</sub> liberated from the sample after adding a strong acid. The CO<sub>2</sub> diffuses across a dialysis membrane. A bicarbonate-carbonate buffer solution containing an indicator dye absorbs the CO<sub>2</sub>. A colorimeter then evaluates the new color, which it converts to a total CO<sub>2</sub> measurement.

Two potential problems exist with this method: (1) the color reagent may change with time, thus the laboratory must frequently check standardization curves; (2) exposure of the sample to air will allow loss of CO<sub>2</sub>, as much as 6 mEq/L in an hour.

Arterial blood gas reports generally include a bicarbonate value. The blood gas machine measures pH and pCO<sub>2</sub> and then calculates a bicarbonate value using the Henderson-Hasselbalch equation. Generally, a concurrent venous total CO<sub>2</sub> content will exceed this value by less than 2 to 4 mEq/L, of which 1 to 2 mEq/L represents the difference between venous and arterial blood; the remaining difference comes from dissolved CO<sub>2</sub>.

**Basic Science**

The kidneys and lungs maintain daily acid-base balance. Understanding this normal physiology allows us to appreciate abnormalities. This discussion refers to bicarbonate rather than total CO<sub>2</sub> content, as we measure total CO<sub>2</sub> content as a surrogate for bicarbonate.

Bicarbonate and carbonic acid constitute the major buffer pair in body fluids. Carbonic acid dissociates into hydrogen ion and bicarbonate with a dissociation constant of  $7.95 \times 10^{-7}$ . Carbonic acid also maintains an equilibrium with H<sub>2</sub>O and CO<sub>2</sub>.



We usually describe dissociation constants and hydrogen ion concentrations as negative logarithms. Thus, the negative logarithm of the dissociation constant equals 6.1. This value is called the pKa. Normal hydrogen ion concentration

equals 40 nanoequivalents/liter, corresponding to a pH of 7.4.

The familiar Henderson-Hasselbalch equation derives from these facts:

$$\text{pH} = 6.1 + \log \frac{[\text{HCO}_3^-]}{[\text{H}_2\text{CO}_3]}$$

Carbonic acid concentration is proportional to the partial pressure of carbon dioxide (pCO<sub>2</sub>) in the blood. Multiplying the pCO<sub>2</sub> by a constant (0.03) estimates the carbonic acid concentration, giving the useful form of the above equation:

$$\text{pH} = 6.1 + \log \frac{\text{HCO}_3^-}{0.03 \times \text{pCO}_2}$$

Changes in hydrogen ion concentration (pH) result from changes in either bicarbonate or carbon dioxide. Measurement of total CO<sub>2</sub> content can help us explain acid-base disorders (when the pH and pCO<sub>2</sub> are known). Furthermore, since we often measure total CO<sub>2</sub> content as part of automated chemistry determinations, this measurement can provide the first clue to acid-base disturbances.

We produce approximately 1 mEq/kg daily of hydrogen ions (derived from metabolism of proteins primarily). The kidney normally excretes this daily acid load. Failure of excretion forces the reaction of H<sup>+</sup> and HCO<sub>3</sub><sup>-</sup>, resulting in a decrease of bicarbonate concentration.

Bicarbonate reabsorption occurs primarily in the proximal tubule. Carbonic anhydrase controls this absorption. The patient's volume status has a major influence on absorption, since sodium is reabsorbed along with this bicarbonate. Thus, volume contraction stimulates both sodium and bicarbonate reabsorption. This results in an increased total CO<sub>2</sub> content. Likewise, volume expansion can lead to a mild decrease in total CO<sub>2</sub> content.

Hydrogen ion concentration (pH) is another major determinant of bicarbonate reabsorption. Thus, the kidney will respond to changes in ventilation (pCO<sub>2</sub>) with compensatory changes in bicarbonate reabsorption. For example, chronic hypoventilation (↑ pCO<sub>2</sub>) causes a decreased pH. This decreased pH stimulates bicarbonate reabsorption, thus the patient will have an increased total CO<sub>2</sub> content.

**Clinical Significance**

The major caveat concerning total CO<sub>2</sub> content involves the interpretation of an isolated measurement. *One cannot diagnose acid-base disturbances from an isolated total CO<sub>2</sub> measurement.* In order to characterize an acid-base disturbance, one needs pH, pCO<sub>2</sub>, total CO<sub>2</sub>, as well as a measurement of the anion gap. Given that caveat, one can use the following guidelines.

**Table 196.1**  
Causes of Increased Anion Gap Metabolic Acidosis

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Lactic acidosis  
Ketoacidosis  
  Diabetic  
  Starvation  
  Alcoholic  
Poisonings  
  Methanol  
  Ethylene glycol  
  Paraldehyde  
  Salicylates  
Renal failure

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**Table 196.2**  
Causes of Normal Anion Gap (Hyperchloremic)  
Metabolic Acidosis

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Diarrhea  
Acetazolamide (Diamox)  
Urinary tract—bowel connections  
Ileal conduit  
Renal tubular acidoses  
  Type I—distal  
  Type II—proximal  
  Type IV—hypoaldosterone  
  Moderate renal failure  
Dilutional acidosis  
Acid administration  
  HCl  
  Hyperalimentation  
  Lysine or arginine chloride

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Low levels of total CO<sub>2</sub> result from either metabolic acidosis or as a compensation to respiratory alkalosis. Bicarbonate levels below 10 mEq/L virtually identify metabolic acidosis as the cause, as compensation for respiratory alkalosis will not drive the bicarbonate that low.

If metabolic acidosis is present, one should distinguish between increased anion gap and nonanion gap acidosis. The simplest formula for the anion gap is:

$$\text{AG} = \text{Na}^+ - (\text{HCO}_3^- + \text{Cl}^-)$$

$$\text{nl} \approx 4\text{--}12 \text{ mEq/L}$$

Table 196.1 lists the differential of an anion gap acidosis. Generally, one does not consider this differential until the

**Table 196.3**  
Causes of Metabolic Alkalosis

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Vomiting  
Diuretic therapy  
Excess mineralocorticoids  
  Hyperaldosteronism  
  Cushing's syndrome  
  Bartter's syndrome  
  Licorice ingestion  
Hypokalemia  
Posthypercapnic  
Volume contraction

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gap exceeds 20 mEq/L. Table 196.2 gives the differential for nonanion gap acidosis.

Similar to the interpretation of a decreased bicarbonate level, an increased bicarbonate level may result from either a metabolic alkalosis or as compensation to respiratory acidosis. Table 196.3 lists the causes of metabolic alkalosis.

In summary, the serum total CO<sub>2</sub> content can give clues to acid–base abnormalities. When used in conjunction with the pH and pCO<sub>2</sub>, this measurement helps us define possible causes of metabolic imbalance, especially in acutely ill patients.

## References

- Bia M, Thier SO. Mixed acid–base disturbances: a clinical approach. *Med Clin North Am* 1981;65:347–61.
- Emmett ME, Narins RG. Clinical use of the anion gap. *Medicine* 1977;56:38–54.
- Gabow PA, Kaehny WD, Fennessey PV, et al. Diagnostic importance of an increased serum anion gap. *N Engl J Med* 1980;303:854–58.
- Kassirer JP. Serious acid–base disorders. *N Engl J Med* 1974;291:773–76.
- Narins RG, Emmett M. Simple and mixed acid–base disorders: a practical approach. *Medicine* 1980;59:161–87.
- Narins RG, Gardner LB. Simple acid–base disturbances. *Med Clin North Am* 1981;65:321–46.
- Oh MS, Carroll HJ. The anion gap. *N Engl J Med* 1977;297:814–17.
- Seldin DW, Rector FC. The generation and maintenance of metabolic alkalosis. *Kidney Int* 1972;1:306–21.